Gene Therapy For Ocular Diseases

April 12, 2013
NIH New Investigator Meeting
Gene Therapy: Charting a Future Course
NIH
Bethesda, MD

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COI Disclosure

- Inventor on patents related to several AAV technologies incl. some novel AAV serotypes which are licensed to several pharmaceutical and biotechnological entities
- Consultancy for GlaxoSmithKline, ReGenX Biosciences, Avalanche Biotech – past, unpaid
- Consultancy for Novartis Institutes of Biomedical Research, GenSight Biologicals – current, paid
- Co-Founder of GenSight Biologicals

Gene … Gene Therapy

- 2008: The Proof of Concept - Bennett, Ali and Hauswirth
  - Safety and Efficacy in subjects affected by LCA2
  - 150+ patients received intraocular AAV
  - 10 Ongoing ocular gene therapy studies, many others preclinical
- 2012-: The Platform
  - NIH Workshop on Gene Therapy: 'Can a platform be developed? … *Using the example of AAV vectors for eye diseases, the discussion focused on factors to be considered in developing a platform for a field in which patients were eager to see the success of the RPE65 trials applied to other LCA or eye disorders. In all of these diseases, the eye will be the target tissue.'*

Clinical trials in retinal gene transfer

Indication	Gene	Vector	ROA	Stage	Center/Sponsor
LCA-RPE65	RPE65	AAV2	SR	Phase I/II (ongoing)	Moorfield Eye Hospital, University College London
				Phase I (completed)	University of Florida/University of Pennsylvania
				Phase I/II (completed) **Phase III (ongoing)**	University of Pennsylvania/ Children's Hospital of Philadelphia
				Phase I (ongoing)	Hadassah Medical Center, Israel
				Phase I/II (ongoing)	Casey Eye Institute, Oregon
Choroideremia	CHM (REP1)	AAV2	SR	Phase I/II (ongoing)	Moorfield Eye Hospital, University College London
Stargardt Disease, AR	ABCA4	EAIV (lenti)	SR	Phase I/II (ongoing)	Oxford Biomedica
Usher 1b	MYO7a	EAIV (lenti)	SR	Phase I/II (ongoing)	Oxford Biomedica
Retinitis Pigmentosa, AR	MERTK	AAV	SR	Phase I/II (ongoing)	Saudi Arabia
Age Related Macular Degeneration, wet form	sFlt-1	AAV2	IVit	Phase I (ongoing)	Genzyme/Sanofi
Age Related Macular Degeneration, CNV	sFlt-1	AAV2	SR	Phase I (ongoing)	Avalanche Bio and Lions Eye Institute, Perth, Australia
Age Related Macular Degeneration, CNV	PEDF	AdV5	IVit	Phase I (completed)	GenVec
Retinoblastoma	HSV-TK	AdV	IVit	Phase I (completed)	Baylor, Houston TX

Gene … Gene Therapy

- 1947-: The Concept - Clyde Keeler - Journal of Heredity
  - 'This has the effect of achieving a permanent correction of hereditary disease…'
- 1986-: The Tools – Muzyczka and Carter - AAV
- 1989-: The Genes – Dryja, Farrar and Cremer – CHM and RHO
- 1994-: The Methods – Bennett - Subretinal Injection
- 2008-: The Proof of Concept - Bennett, Ali and Hauswirth
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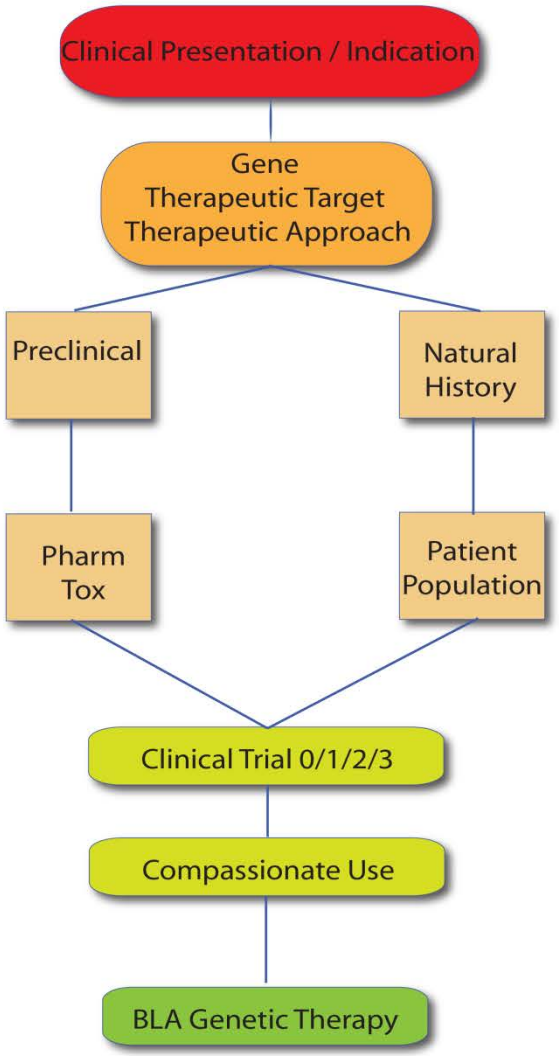
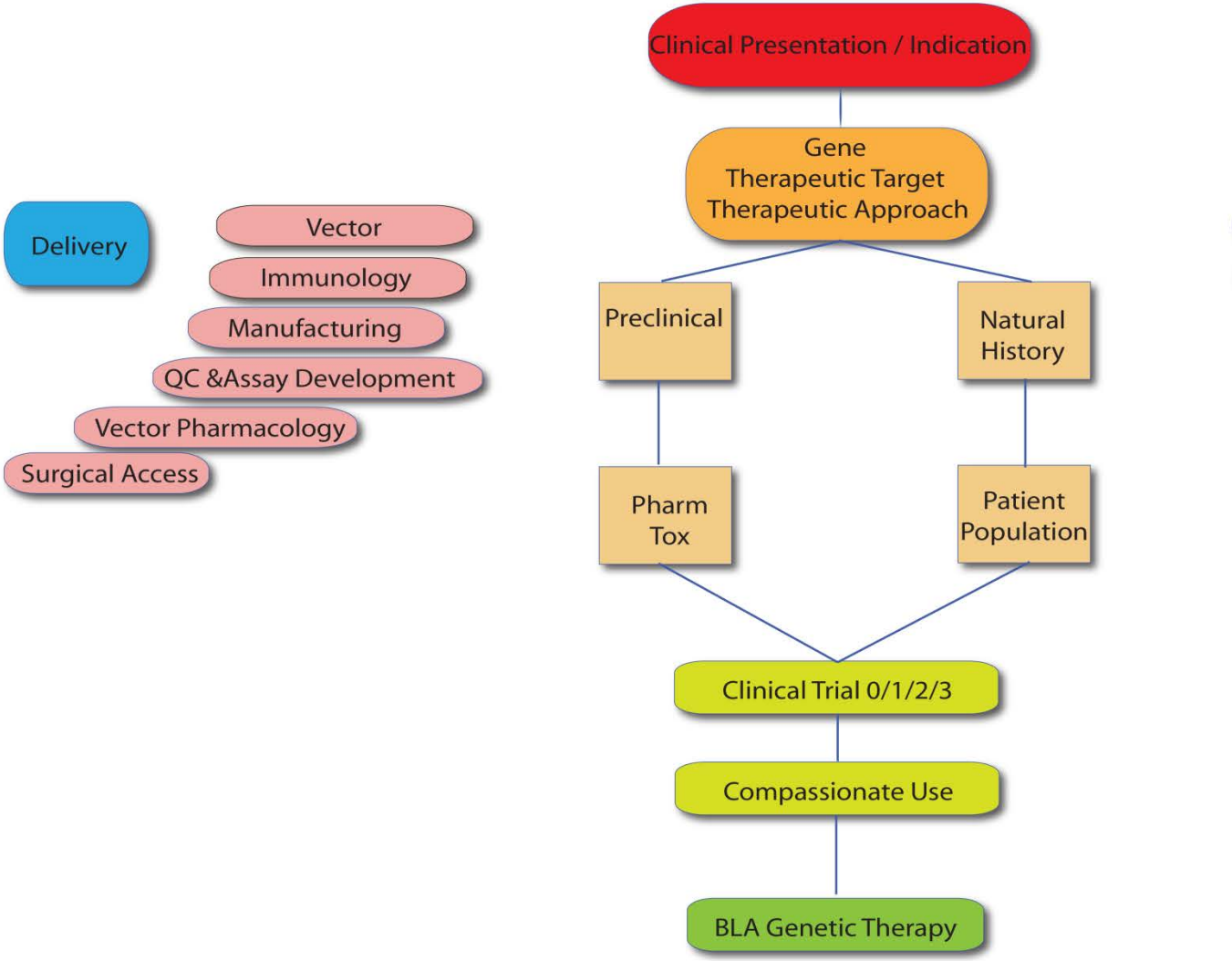
Building a Platform

Building a Platform



Building a Platform



Delivery

- Resources
  - GMP material
- Pharmacological
  - Assays: Identity, Purity, Potency
  - Pharmacokinetics
- Technology
  - Large genomes
  - Targets, Specificity
  - ROA
  - Manufacturing
  - Controlled / Regulated Expression

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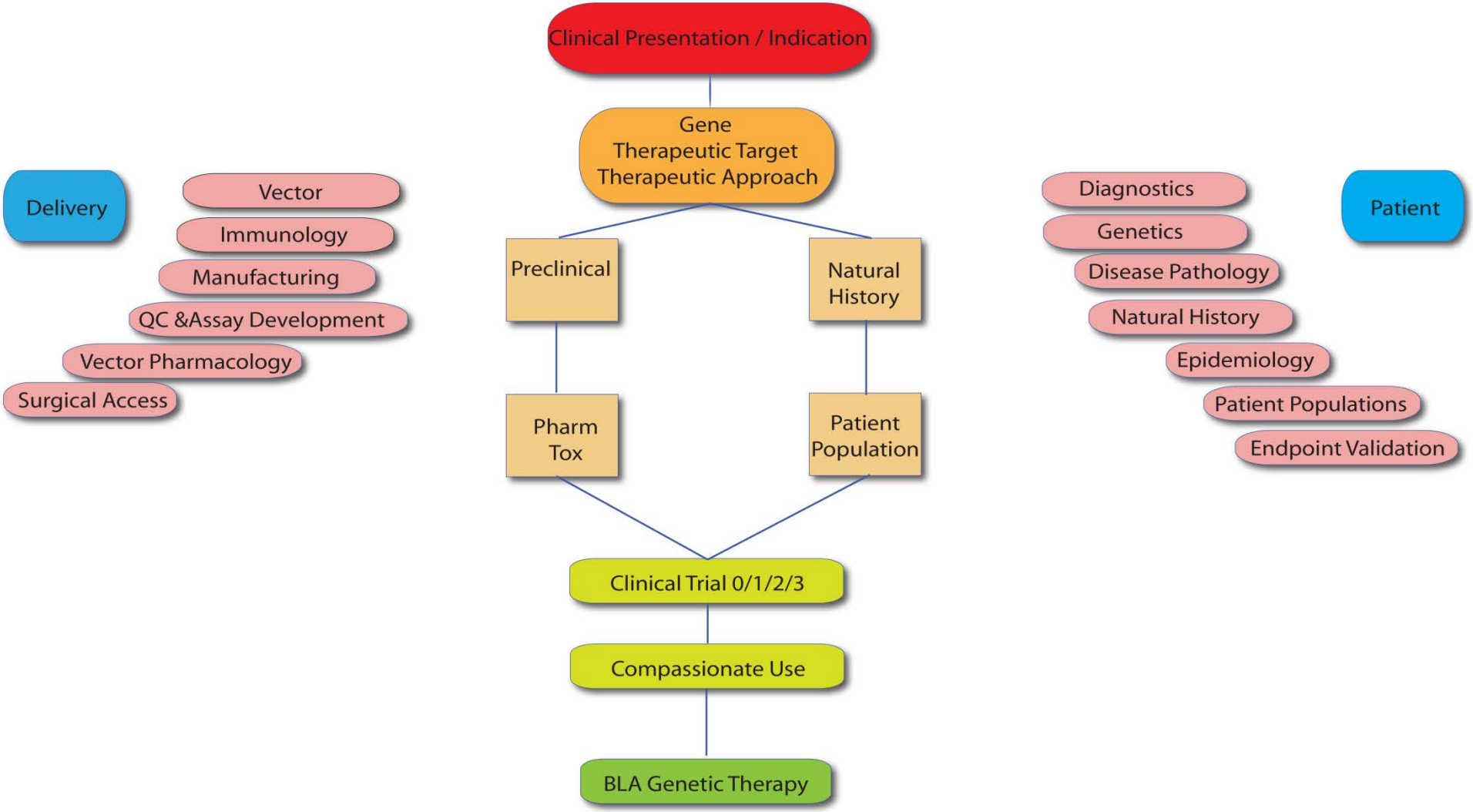
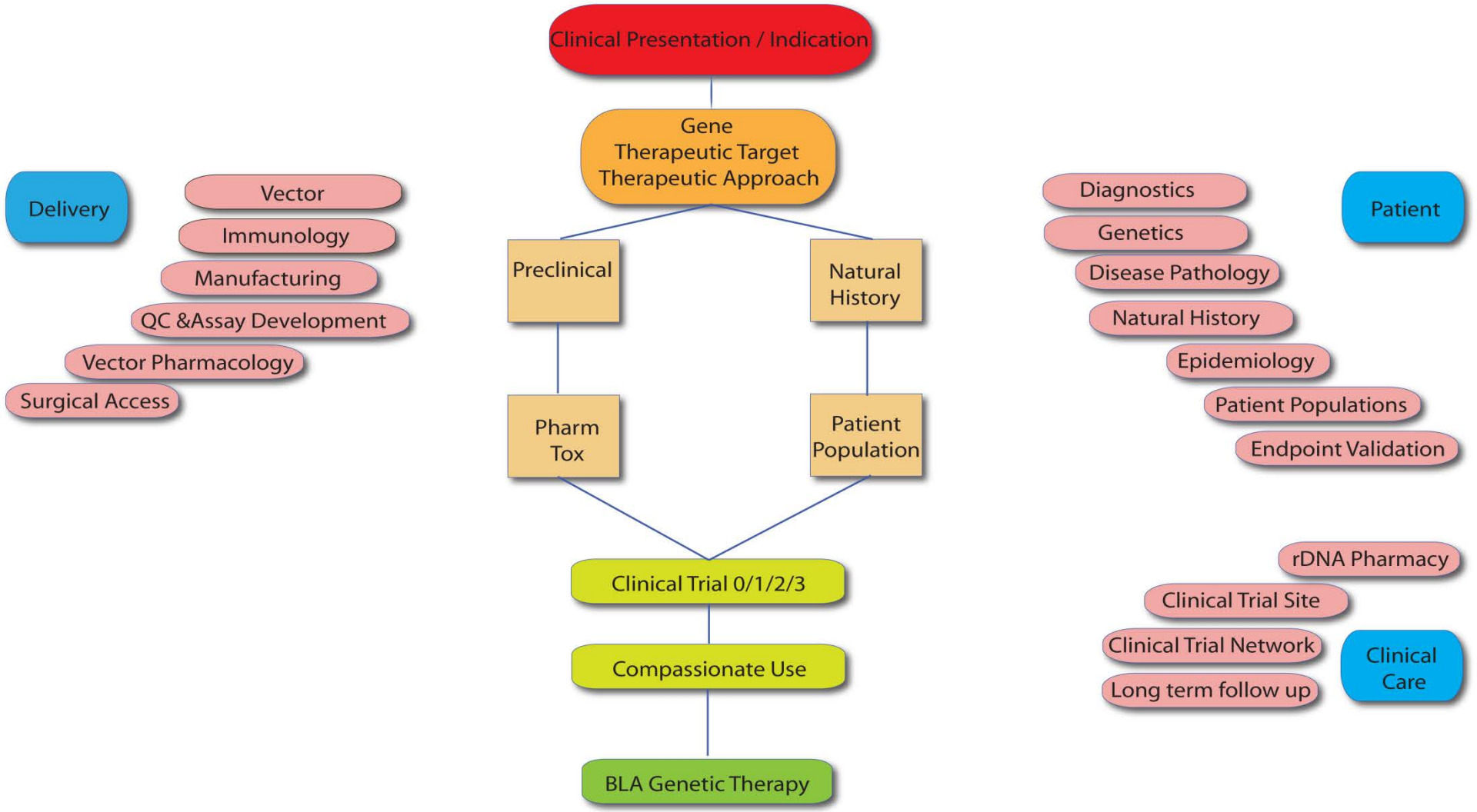


Patient/Disease

- Early Endpoints and Biomarkers
- Natural History
- Disease Pathology and Therapeutic Effect
- Clinical Trial Design – Patient selection

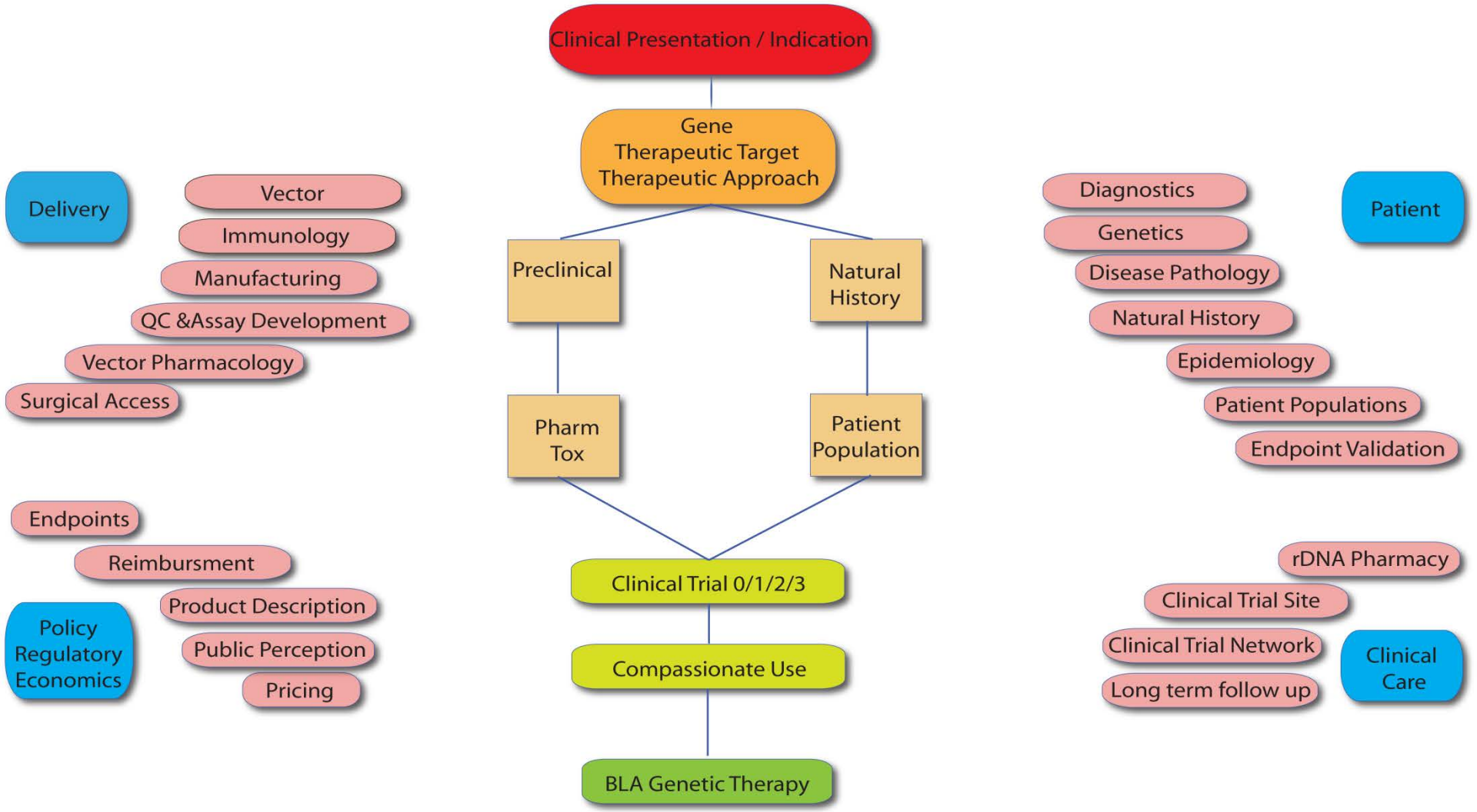
Building a Platform



Clinical Care

- Balancing Clinical Practicality and Outcome
- Standard of Care

Building a Platform



Policy / Regulatory / Economics

- Traction from private sector
- Incentivize single intervention pharmaceutical therapies
- Reduce Cost of Clinical Trials
- Pricing, Reimbursements, Payers
- Broaden Patient populations
  - One gene, one drug
- IP
  - Value before $